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14. ABSTRACT

This proposal studies the role of NF1 in mediating long-term memory retrieval in Drosophila. Over the last funding period, we devoted our efforts in two areas as (1) to determine the role of NF1 in retrieval of LTM and (2) to map neural circuits involved in aversive and appetitive memory retrieval. We made extensive efforts in figuring out problems we encountered in rescuing the NF1-dependent memory phenotype and now we are back to continue the proposed work. For mapping circuits involved in retrieval, we found that γ and α/β lobes, but not α′/β′ lobes, are involved in retrieval of either aversive or appetitive memory. This finding advances current understanding and also provides a basis for studying roles of NF1 in memory retrieval.

15. SUBJECT TERMS
NF1, Drosophila, memory, retrieval, mushroom-body

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Table of Contents

Introduction

We have reported that NF1 affect both immediate memory and long-term memory (LTM), but through different mechanisms in Drosophila (Ho et al., 2007). The major hypothesis we are going to test in this proposal is of that the NF1 gene mediates memory retrieval, but is not required for induction of LTM. For this purpose, three specific aims are proposed, including (1) to determine NF1's role in memory retrieval; (2) to identify ligands that activate NF1 for memory retrieval; and (3) to locate the brain region at which NF1-dependent memory retrieval occurs.

Body

During the first funding year of this grant (2010-2011), we encountered difficult in replicate memory phonotypes reported in the preliminary observations of this proposal, largely due to personnel changes—departure of senor graduate student and taking over the project by a freshman graduate student who had significant gap in time with the senior student. The newly involved graduate student was capable of showing mutant defects in learning and memory, but was unable to rescue such phenotype with expression of transgenes (reported in the last progress report).

Over last funding period (2011-2012), we were continuing to make efforts in verifying the NF1's role in memory retrieval. After extensive efforts in verifying the genetic background and reestablish the appropriate genotypes, this problem was finally resolved to some extends. The student was able to show that the NF1P2 learning and memory defect was rescued through elav-Gal4 (pan-neuronal driver) driven expression of the NF1 transgene (Fig. 1). Now the student is making efforts to establish rescue of the learning and memory NF1 mutant phenotypes through acutely induced NF1 transgene expression, which is necessary in demonstrating a critical role for NF1 in memory retrieval.

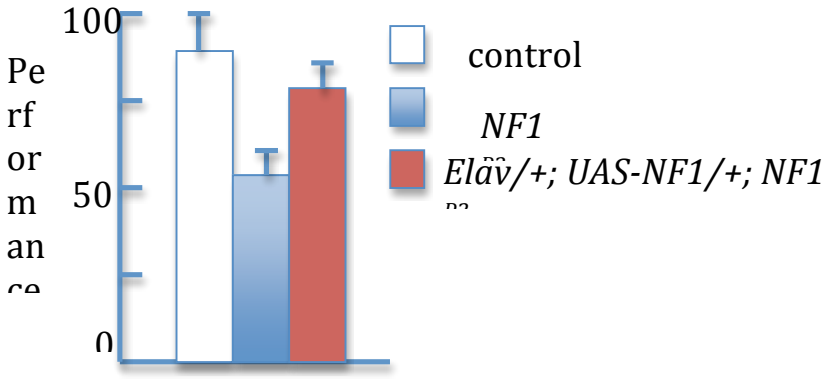

Fig. 1 Rescue of the NF1 learning defect through elav-gal4 driven expression of NF1 transgene. N=6,8,6 for control, NF1P2, and elav;UAS-NF1;NF1P2, respectively.

In parallel with the effort in directly relevant to NF1's role, we also made major efforts in mapping neural circuits that are important for retrieval of memory, during last funding period, which was proposed as part of work in the Specific Aim 3. Our preliminary data suggest that both γ and α/β lobes of the mushroom body (MB), but not α′/β′ lobes, are involved in retrieval of 3hr memory (Figs 2 and 3). This observation is in conflict from published results (Trannoy et al., 2011), which reports that only the γ lobe is needed for retrieving appetitive memory while the α/β lobes are necessary for aversive memory. Such discrepancy may arise from different Gal4 lines used. We have identified one a new Gal4 line that is strongly enriched in the γ lobe. We are continuing to work on long-term memory retrieval and whether NF1's function in retrieval is confined to such neural circuit.

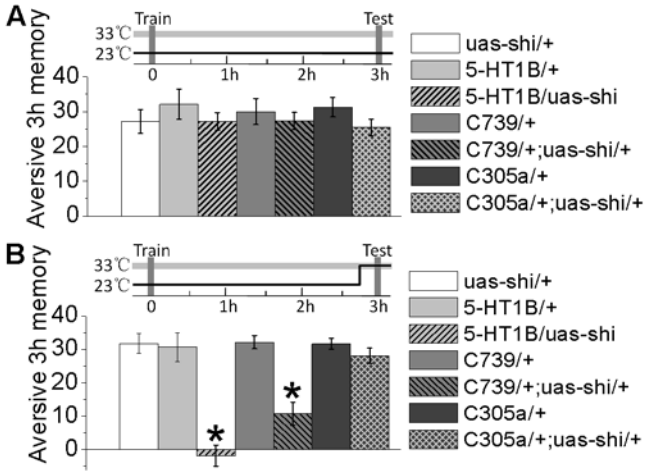

Fig. 2. Blocking the output from γ lobe or α/β lobes impairs the retrieval of aversive 3h memory. (A) When constantly under the permissive temperature of 23° C, all genotypes showed normal aversive 3h memory performance. (B) Blocking the output from 5-HT1B-Gal4 labeled γ lobe neurons under the restrictive temperature of 33° C completely abolished aversive 3h memory retrieval. Blocking the output from C739 labeled α/β lobe neuron also impaired memory retrieval. In all groups, N≥8. All error bars indicate SEM. * denotes $p<0.05$.

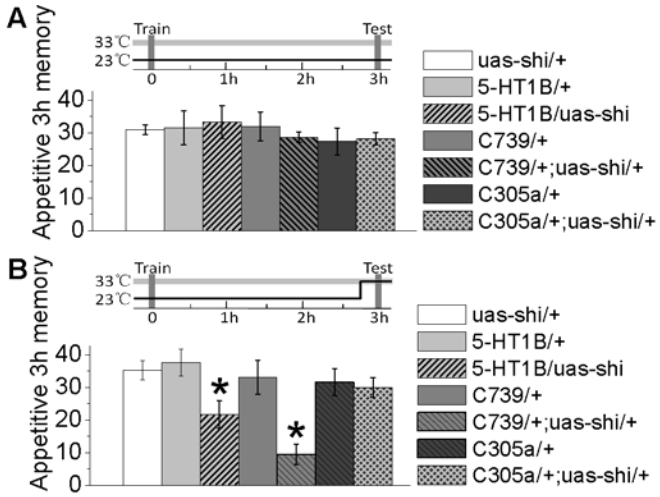

Fig. 3. γ lobe and α/β lobes are both required for the retrieval of appetitive 3h memor y. (A) When constantly under the permissive temperature, all genotypes showed normal appetitive 3h memory performance. (B) Blocking the output of 5-HT1B-Gal4 labeled γ lobe or C739-Gal4 labeled α/β lobe, but not C305a labeled α'/β' lobe, impaired appetitive 3h memory retrieval. In all groups, N≥8. All error bars indicate SEM. * denotes $p<0.05$.

Key Research Accomplishments

We identified that both γ and α/β lobes of the mushroom body, but not α′/β′ lobes, are involved in retrieval of 3hr memory. This result provides a foundation for determining NF1's role in memory retrieval.

Reportable Outcomes

There is no reportable outcome directly related to proposed NF1 work.

Conclusion

(1) Through an extended period of struggling, we finally believe we can get back on track to test NF1-mediated memory retrieval and will continue to work on Task 1 and 2 in the coming funding period.
(2) We identified that both γ and α/β lobes of the mushroom body, but not α′/β′ lobes, are involved in retrieval of 3hr memory.

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